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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/813,829	03/06/97	HOGAN	B 16016.0005

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EXAMINER	
CLARK, D	
ART UNIT	**PAPER NUMBER**
1633	8

DATE MAILED: 07/02/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/813,829	Hogan, B. L. M.
Examiner	**Group Art Unit**
Deborah Clark	1633

☒ Responsive to communication(s) filed on *Mar 29, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-4* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I without traverse in paper no. 6 has been received 03/29/99.

Response to Amendment

2. Applicant's amendment has been received, 03/29/99. Claims 1-4 are now pending.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mouse embryonic stem cells, does not reasonably provide enablement for mammalian non-murine embryonic stem cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to make or use non-murine embryonic stem cells. The nature of the claimed invention is embryonic stem (ES) cells. By

definition, embryonic stem cells are able to contribute to all tissues of an animal including the germ cells (see Nichols et al., page 1341, ¶ 1). The state of the art of the claimed invention is not well established. In May of 1992, Bradley et al. states that at the time ES cells were known only for the species mouse (see the ¶ bridging pages 537-538). In 1993, Wheeler describes isolation of porcine embryonic stem cells (though using a different method than that taught by applicants) (see US 5,523,226, throughout, especially claim 4). The art of isolating ES cells is highly unpredictable. Cruz et al. list some of the differences in early embryonic development among swine, oxen, horses, goats, and sheep (see Table 1, page 166). Piedrahita et al. observed that porcine and ovine embryos responded differently to the same treatments. Conditions that allowed production of porcine ES-like cell lines did not allow development of ovine ES-like cell lines (see Table 1, page 886, and page 888). Therefore, one cannot extrapolate from procedures shown effective in one species to another species. As demonstrated by the art cited above numerous attempts have been made to isolate ES cells from species other than the mouse, but (other than the porcine ES cells as claimed by Wheeler) demonstration that these cells are able to contribute to the germ line is awaited (see Clark et al., page 250, ¶2). The guidance set forth in the specification is not sufficient to enable one of skill in the art to isolate non-murine mammalian ES cell lines. The specification sets forth a procedure for the isolation of ES cells. However, this procedure has been shown as successful only for mice. The working examples set forth demonstrate that a mouse ES cell line was established. The working examples also demonstrate that human ES-like cells were isolated, however, these cells were not demonstrated to be true ES

cells. The breadth of the claims is not enabled because the claims encompass all non-murine mammalian species and ES cells. The amount of experimentation required to practice the claimed invention commensurate in scope with the claims is paramount. It is not clear that the successful procedure used in the mouse species would be successful in any other species. In addition, the amount of experimentation required to demonstrate that ES-like cells are true ES cells is vast because the ES-like cells would need to be implanted into a blastocyst, allowed to grow to term, and then demonstrated to have true mosaicism in all tissues including germ line cells.

Therefore, given the nature of the claimed invention, the state of the art, the level of predictability found in the art, the guidance set forth in the specification, the working examples set forth in the specification, the breadth of the claims, and the amount of experimentation required to practice the invention as claimed, practice of the invention commensurate in scope with the claims would require undue experimentation on the part of the skilled artisan.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 4 recite the phrases "cell phenotypes" and "essential characteristics". These phrases render the claims indefinite.

The phrase "multiple differentiated cell phenotypes" is indefinite because the phrase is grammatically incorrect and cannot be read in any manner which makes clear to the skilled artisan what is required of the cells. The phrase should be amended to recite "differentiated cells with multiple phenotypes" or the like.

The phrase "essential characteristics" renders the claims indefinite because it is not clear which characteristics are deemed essential. Therefore, the skilled artisan is not apprised as to the scope of the claimed invention.

Claims 2 and 3 are rejected for the reasons set forth above because they depend from claim 1.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 5,453,357. Although the

conflicting claims are not identical, they are not patentably distinct from each other because the claims are co-extensive. The claims herein are directed to mammalian non-murine, or human, ES cells. The claims of '357 are directed to a composition comprising ES cells (of any species) and certain specific media components. Therefore, the claims of '357 would encompass the invention claimed herein when the cells claimed herein are cultured with those media components. Likewise, the claims herein encompass the cells of the composition where the cells are non-murine.

It is noted that applicants have filed a terminal disclaimer over US Patent No. 5,690,926, however, no disclaims has been filed over US Patent No. 5,453,357.

Priority

9. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

> The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

Applicant's disclosure as set forth in the 07/958,562 is insufficient to comply with the requirements of the first paragraph of 35 USC 112, 1st paragraph in regards to the invention

claimed herein. The nature of the invention, state of the art, predictability of the art, and breadth of the claims is set forth above. The guidance and working examples set forth in '562 is not sufficient to enable the claimed invention. The guidance set forth in '562 sets forth the same procedure as set forth herein. The working examples set forth in '562 merely demonstrates the successful isolation of mouse ES cells. Therefore, based upon the nature of the invention, the state of the art, the level of predictability found in the art it is concluded that the guidance and working examples cannot be taken as enabling for the full breadth of the claimed invention. Specifically, the breadth of the claims that was enabled in '562 is excluded from the claimed invention.

Therefore, the priority granted to the claimed invention is 03/25/94, the date of the filing of application no. 08/217,921.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Wheeler, US Patent No. 5,523,226.

Claim 1 is directed to a mammalian non-murine ES cell. Claim 2 is directed to the ES cell of claim 1 which has a mutation which renders a gene non-functional. Claim 3 is directed to the ES cell of claim 1 which has an insertion of a functional gene.

Wheeler discloses porcine ES cells and demonstrates that they are in fact true ES cells (see throughout, especially claim 4 and col. 22). Wheeler teaches methods for introducing genes into the ES cell for production of protein in a transgenic animal or removing of altering deleterious genes where specific DNA sequences are removed from the ES cell (see cols. 17-19). Therefore, the claimed invention is anticipated.

Though the claim recites certain features of the cells, all true ES cells are considered to inherently have the same features. Further, though the ES cells are stated to have been derived from PGCs, it is not clear that the resultant product claimed herein would be any different than the prior art product. This is similar to a product-by-process type limitation. In such case, see MPEP 2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe , 227 USPQ 964, 966 (Fed. Cir. 1985). The USPTO does not have the facilities to compare the cells, thus, applicants should provide evidence which clearly distinguishes the disclosed cells from those known in the art.

Conclusion

12. No claim is allowed.

13. Claim 4 is free of the prior art of record because the prior art does not disclose human embryonic stem cells.

14. The signature of the group director indicates his concurrence with these rejections.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Clark whose telephone number is (703) 305-4051. The examiner can normally be reached on Mondays-Fridays from 7:10 a.m. EST to 3:40 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Stanton, can be reached on (703) 308-2801. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DRC

06/28/99

Deborah Crouch

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PRIMARY EXAMINER
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